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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,660	04/21/2004	Ahmad Khalaf Al-Deeb Al-Ghazawi	P32151-1 Div1-C2	4924

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GLAXOSMITHKLINE
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939

EXAMINER	
CHANG, CELIA C	
ART UNIT	PAPER NUMBER
1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,660	AL-GHAZAWI ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 April 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This application is a continuation of SN 09/803,789. A preliminary amendment was filed canceling claims 1-33. Claims 34-48 are pending and examined.

2. Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Complete revision of the content of the abstract is required on a separate sheet.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benneker et al. US 5,874,447 (cited on 1449) in view of Jacewicz GB 2,297,550 (1449), Fox and Pathak et al. WO 95/16448.

Determination of the scope and content of the prior art (MPEP §2141.01)

Benneker et al. '447 disclosed the active compound of the claims (see col.7 example 1) in oral pharmaceutical composition (see col. 7, lines 8-13) as conventionally prepared.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Benneker et al. '447 disclosed all the elements of the claims **except** the IR data, the quantity of active ingredient or the name/function of the carrier have not been specified but disclosed as conventionally known in the art. Jacewicz et al. explicitly taught the preferred unit dosage of paroxetine, which is the active ingredient of the instant composition (see p.9, line 12). Fox taught that IR data are purity indicator i.e. material with IR data differ from those without by degree of purity. Pathak et al. '448 taught the particular elements of the oral tablet carrier of the claims (see p.3).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art is deemed to be aware of all the pertinent art in the field. The above references place the conventional carrier and dosage information in the possession of artisan together with the general teaching of Benneker '447 of the particular salt form of paroxetine. A skilled person would be motivated by Benneker's guidance to employ Benneker's paroxetine methane sulfonate with the conventional dosage and carrier which is the instant claimed composition. The IR spectrum of the claims is not a limitation but an inherent feature of the compound. Thus if the compound of Benneker '447 is identical to the instant claims, then, it would inherently have the same IR. The IR spectrum is known to be a purity indicator, thus, if Benneker's compound has a different IR, it differs from the claims only by degree of purity i.e. a prima facie obvious variation.

Applicants argued that different IR indicates different polymorphic form, thus, indicated difference between the claims and material disclosed by Benneker. Please note that, the rejection is that different IR of the same product indicated that they are the "same" product with different physical property. It has been explained that based on definition of purity as evidence by Fox, skilled person in the field would consider that the difference in "physical characteristic" corresponding to the difference in impurity, thus, would indicate that such difference from is a mere variation of the same product. Applicants have provided no factual evidence other than alleging to be a polymorphic form to show that such polymorphic forms, which are mere physical variation of the same compound, would have any unexpected property that was not inherent in or rendered obvious by the prior art. In re Cofer 148 USPQ 268.

4. Claims 34-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. .In evaluating possession of the claims, the following analysis was made:

--a complete review of the state of the art with many references indicating the necessity of explicit and specific guidance for preparing pharmaceutical composition maintaining crystallinity of the active agent (see Muzaffar, Jain, doelker or Otsuke below) ;

--a complete review of the specification which disclosed liquid preparation and one dry direct compression for which no information about crystallinity after process was provided ;

--a complete review of the skill level of artisan in the field providing that the field is well aware of preserving crystallinity proper solid carrier, proper compression condition, etc. must provided for such composition to be available (see Muzaffar, Jain, Doelker or Otsuke provided;

--a complete review of the unpredictability and empirical nature of the art, see i.e. Tricky business, indicated without explicit specific disclosure, one having ordinary skill has not been offer description of what "is" the composition.

The Office has met the burden of establishing a prima facie case of lacking sufficient description based on the complete review of the specification in view of the state of the art.

5. Claims 34-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id.* An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id.* at 740, *Id.* at 1407. The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

In evaluation of enablement, it is clearly delineated that:

Nature of invention

The field of pharmaceutical composition of crystalline product is highly unpredictable and empirical.

The state of the art and predictability

See :

Muzaffar et al. p.60 "At any one temperature and pressure only one crystal form of a drug is stable and any other polymorph existing under these conditions will convert to the

stable form .... " And p.63-65 (a)-(h) pharmaceutical preparing processes affect polymorphism;
Jain et al. p.322-326, manufacturing processes that affect polymorphs ;
Doelker et al. abstract, "One may also observe changes in technology or pharmaceutical properties that are due to polymorphic environmental conditions undergone by the product or the dosage form"
Doelker et al. abstract "...a given drug, although chem. well defined, may exhibits quite different behavior. Process conditions (grinding, tableting, granulations, drying) may also affect secondary properties of the drug, such as compactibility, wetttability, soly, dissolution rate, bioavailability and even pharmacological, activity."
Otsuke et al. p.852 ~ ...in formulation studies and the method preparing CBZ has been shown to affect the drug's pharmaceutical properties through the polymorphic phase transformation of the bulk CBZ powder during the manufacturing process"

The amount of guidance and working examples
On page 55, direct compression tablets of paroxetine mesylate was disclosed but no information as to the maintenance of crystallinity in the composition was found.

The Office has met the burden of establishing a prima facie case of lacking sufficient enablement based on the unpredictable nature of the product disclosed by the specification in view of the state of the art.

There is no factual support in the record that the instant "form" would be *out of the ordinary and be spontaneously maintained* in a composition while ordinary skill in the art well recognized the need to invest tremendous effort in establishing specific conditions in obtaining such a composition (see Trick business).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner can be reached by facsimile at (703) 308-7922 with courtesy voice message supra.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

OACS/Chang
Feb. 12, 2007

Celia Chang
Primary Examiner
Art Unit 1625